

Patent claims

1. A method for generating a genetically modified organism for drug screening, which comprises the steps
5
a) causing heterologous expression of at least one protein or protein fragment by genetic modification of the organism
b) analyzing the modified gene expression pattern and identifying
10 compensatingly differentially regulated genes
c) phenotyping the organism.
2. The method as claimed in claim 1, wherein phenotyping is carried
15 out by reducing/eliminating the compensatingly differential expression or by labeling at least one compensatingly differentially regulated gene.
3. The method as claimed in either of claims 1 and 2, wherein the
20 genetic modification causes heterologous expression of at least one protein or protein fragment which is endogenous to the organism and/or foreign.
4. The method as claimed in any of claims 1 to 3, wherein the genetic
25 modification causes reduction or elimination of the expression of at least one protein endogenous to the organism.
5. The method as claimed in any of claims 1 to 4, wherein the modified
expression is inducible.
6. The method as claimed in claim 5, wherein the genetic modification
30 comprises introducing a vector which enables the protein or protein fragment to be inducibly expressed, preferably a vector inducible with galactose, copper tetracycline or other comparably inducible vectors.
7. The method as claimed in any of claims 1 to 6, wherein the genetic
35 modification comprises a knock out, preferably an inducible knock out.
8. The method as claimed in any of claims 1 to 7, wherein the organism is drosophila, C. elegans, a prokaryotic or a eukaryotic cell.

9. The method as claimed in claim 8, wherein the cell is a yeast cell, preferably a yeast cell of the strain *S. cerevisiae*.

5 10. The method as claimed in any of claims 1 to 9, wherein the modified gene expression is analyzed with the aid of DNA or protein microarrays.

10 11. The method as claimed in any of claims 1 to 10, wherein phenotyping is carried out by reducing or eliminating expression of the compensatingly differentially regulated gene.

12. The method as claimed in claim 11, wherein expression of the compensatingly differentially expressed gene is enhanced to control organisms and the reduction or elimination is caused by at least partial inhibition of said enhanced expression.

15 13. The method as claimed in claim 7, wherein the knock out of the differentially expressed gene is carried out [lacuna] replacing at least part of the coding sequence of the differentially regulated gene with the coding sequence of a reporter gene or parts of the reporter gene sequence which are sufficient to be detected.

20 14. The method as claimed in claim 11, wherein the differentially expressed gene is less strongly expressed than in control organisms and the reduction or elimination is carried out by enhancing its expression.

25 15. The method as claimed in any of claims 1 to 14, wherein the reduction or elimination leads to growth inhibition of the organism.

30 16. The method as claimed in any of claims 1 to 10, wherein phenotyping is carried out by labeling the gene product of the compensatingly differentially regulated gene.

35 17. A genetically modified, phenotype organism, obtained by a method as claimed in any of claims 1 to 16.

18. A genetically modified organism, having

a) genetically modified expression of at least one endogenous or foreign gene, which results in compensatingly differential expression

of at least one other gene endogenous to said organism, and

- 5 b) a phenotype caused by reducing/eliminating the compensatingly differential expression of the gene or by labeling the compensatingly differentially regulated gene product.

10 19. The use of a genetically modified organism as claimed in either of claims 17 or 18 for screening for substances having an effect on the function of the heterologous protein or protein fragment.

15 20. A method for identifying substances having an effect on the function of the heterologously expressed protein or protein fragment, which method comprises the use of the organism as claimed in either of claims 17 or 18.

20 21. An assay for drug screening using at least one phenotype organism as claimed in either of claims 17 or 18, which comprises the steps

25 c) determining the phenotype of said organism

30 d) contacting the substance to be tested with said organism

35 e) observing a possible modification of said phenotype.

40 22. A substance, which is identified by a method as claimed in claim 20 or an assay as claimed in claim 21 as a substance which at least reduces the phenotype.